L6 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:654747 CAPLUS
DOCUMENT NUMBER: 135:222364
TITLE: DNA sequence of human prostaglandin E2 receptor 1 (**EP1-R**) gene, and methods for the diagnosis of **polymorphisms** thereof
INVENTOR(S): Smith, John Craig; Anand, Rakesh; Morten, John Edward Norris
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1130122	A2	20010905	EP 2001-301291	20010213
EP 1130122	A3	20011017		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002076702	A1	20020620	US 2001-781311	20010213
JP 2001286288	A2	20011016	JP 2001-40076	20010216

PRIORITY APPLN. INFO.: GB 2000-3553 A 20000217
GB 2000-8376 A 20000406

AB The invention provides the genomic DNA sequence of the human prostaglandin E2 receptor 1 (EP1-R) gene; it differs from the cDNA sequence of EMBL L22647 and the DNA sequence of EMBL AC008569. The invention also provides methods of diagnosing fourteen specific **polymorphisms** in the **EP1-R** gene and novel allelic polypeptides encoded thereby. The invention provides allele-specific probes and/or primers for use in diagnosis. The invention also relates to methods of diagnosis and treatment of EP1-R ligand mediated diseases, such as cancer or arthritis.

L10 ANSWER 16 OF 17 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2000005672 MEDLINE
DOCUMENT NUMBER: 20005672 PubMed ID: 10537280
TITLE: Role of the **prostaglandin** E **receptor** subtype **EP1** in colon carcinogenesis.
AUTHOR: Watanabe K; Kawamori T; Nakatsugi S; Ohta T; Ohuchida S; Yamamoto H; Maruyama T; Kondo K; Ushikubi F; Narumiya S; Sugimura T; Wakabayashi K
CORPORATE SOURCE: Cancer Prevention Division, National Cancer Center Research Institute, Tokyo, Japan.
SOURCE: CANCER RESEARCH, (1999 Oct 15) 59 (20) 5093-6. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991110

AB Although the cyclooxygenase pathway of the arachidonic acid cascade has been suggested to play an important role in colon carcinogenesis, the molecular species of prostanoids and receptors involved have not been fully elucidated yet. We examined the development of aberrant crypt foci (ACFs), putative preneoplastic lesions of the colon, in two lines of knockout mice, each deficient in **prostaglandin** E **receptors**, **EP1** and EP3, by treatment with the colon carcinogen, azoxymethane. Formation of ACFs was decreased only in the EP1-knockout mice to approximately 60% of the level in wild-type mice. Administration of 250, 500, or 1000 ppm of a novel selective EP1 antagonist, ONO-8711, in the diet to azoxymethane-treated C57BL/6J mice also resulted in a dose-dependent reduction of ACF formation. Moreover, when Min mice, having a nonsense mutation in the adenomatous polyposis coli gene, were given 500 ppm ONO-8711 in the diet, the number of intestinal polyps was significantly reduced to 57% of that in the basal diet group. These results strongly suggest that prostaglandin E2 contributes to colon carcinogenesis to some extent through its action at the EP1 receptor. Thus, EP1 antagonists may be good candidates as chemopreventive agents for colon **cancer**.

OF 19 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002179026 MEDLINE
DOCUMENT NUMBER: 21908116 PubMed ID: 11911260
TITLE: Evaluation of a selective prostaglandin E receptor EP1 antagonist for potential properties in colon carcinogenesis.
AUTHOR: Kawamori T; Uchiya N; Kitamura T; Ohuchida S; Yamamoto H; Maruyama T; Sugimura T; Wakabayashi K
CORPORATE SOURCE: Cancer Prevention Division, National Cancer Center Research
Institute, Tokyo, Japan.. tkawamor@gan2.ncc.go.jp
SOURCE: ANTICANCER RESEARCH, (2001 Nov-Dec) 21 (6A) 3865-9.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020326
Last Updated on STN: 20020420
Entered Medline: 20020419

AB BACKGROUND: Cyclooxygenases (COXs) and prostanoids play pivotal roles in colon carcinogenesis. This study was designed to determine the chemopreventive effects of ONO-8711, a selective prostaglandin E receptor EP1 antagonist, on the development of azoxymethane (AOM)-induced colonic aberrant crypt foci (ACF) in male F344 rats and to compare its potential with that of nimesulide, a well-documented selective COX-2 inhibitor. MATERIALS AND METHODS: Five-week-old male F344 rats received s.c. injections of AOM (15 mg/kg body weight) or the saline vehicle once weekly for two weeks and were fed the control diet (AIN-76A) or the experimental diets containing 400 or 800 ppm of ONO-8711 or 400 ppm nimesulide for 5 weeks. RESULTS: Administration of ONO-8711 at 800 ppm significantly reduced the total number of ACF/colon and 5-bromodeoxyuridine (BrdUrd) labeling index as compared to the control diet group (by 31% and 66%, respectively). As expected, dietary administration of nimesulide also suppressed the development of ACF and BrdUrd labeling index in the colon, by about 39% and 54%, respectively. CONCLUSION: Our finding that ONO-8711 significantly suppresses colonic ACF formation and cell proliferation strengthens the hypothesis that the selective **prostaglandin** E **receptor EP1** antagonists possesses chemopreventive **activity** against colon cancer development.

RESULT 1
AC008569/c
LOCUS AC008569 227245 bp DNA linear PRI 05-SEP-2001
DEFINITION Homo sapiens chromosome 19 clone CTC-548K16, complete sequence.
ACCESSION AC008569
VERSION AC008569.7 GI:15431055
KEYWORDS HTG.
SOURCE human.
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 227245)
AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.
TITLE Direct Submission
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 227245)
AUTHORS DOE Joint Genome Institute.
TITLE Direct Submission
JOURNAL Submitted (03-AUG-1999) Production Sequencing Facility, DOE Joint Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA
REFERENCE 3 (bases 1 to 227245)
AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.
TITLE Direct Submission
JOURNAL Submitted (08-NOV-2000) DOE Joint Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA
REFERENCE 4 (bases 1 to 227245)
AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.
TITLE Direct Submission
JOURNAL Submitted (05-SEP-2001) DOE Joint Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA
COMMENT On Sep 5, 2001 this sequence version replaced gi:11120757.
Draft Sequence Produced by DOE Joint Genome Institute
www.jgi.doe.gov
Finishing Completed at Stanford Human Genome Center
www-shgc.stanford.edu
Quality: Phrap Quality >=40 99.8% of Sequence;
Estimated Total Number of Errors is 0.3.
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SHGC-141627 G63606
SHGC-35463 G29823
SHGC-31833 G29335.
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/clone="CTC-548K16"
BASE COUNT 54928 a 59916 c 58482 g 53919 t
ORIGIN

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RESULT 4
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LOCUS HUMG 1376 bp mRNA linear PRI 03-JAN-1994
DEFINITION Human prostaglandin receptor ep1 subtype mRNA, complete cds.
ACCESSION L22647
VERSION L22647.1 GI:410208
KEYWORDS prostaglandin receptor ep1 subtype.
SOURCE Homo sapiens cDNA to mRNA.
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 1376)
AUTHORS Funk,C.D., Furci,L., FitzGerald,G.A., Grygorczyk,R., Rochette,C.,
Bayne,M.A., Abramovitz,M., Adam,M. and Metters,K.M.
TITLE Cloning and expression of a cDNA for the human prostaglandin E
receptor EP1 subtype
JOURNAL J. Biol. Chem. 268 (35), 26767-26772 (1993)
MEDLINE 94075377
REFERENCE 2 (bases 1 to 1376)
AUTHORS Funk,C.D.
TITLE Direct Submission
JOURNAL Submitted (01-NOV-1993) Colin D. Funk, Department of Pharmacology,
Vanderbilt University, Nashville, TN 37232, USA
FEATURES Location/Qualifiers
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5'UTR 1. .74
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LGAVSNLLALALLAQAAGRLRRRRSATTFLLFVASLLATDLAGHVIPGALVLRLYTAG
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VAAVALAVALLPLARVGRYELQYPGTWCFIGLGPPGGWRQALLAGLFASLGLVALLAA
LVCNTLSGLALHRARWRRRSRRPPPASGPDSRRRWGAHGPRSASASSASSIASASTFF
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polyA_signal 1358. .1363
BASE COUNT 138 a 526 c 484 g 228 t
ORIGIN

Query Match 24.7%; Score 967; DB 9; Length 1376;
Best Local Similarity 97.0%; Pred. No. 9.8e-101;
Matches 985; Conservative 0; Mismatches 30; Indels 0; Gaps 0;

Qy 2051 ccagcacccctggcgcctgacatgagcccttgcgggcccctcaacctgagcctggcgggc 2110
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Db    414 GGCGGCTGCATGGTCTTCTTCGGCCTGTGCCCGCTGCTGCTGGGCTGTGGCATGGCCGTG 473

Qy   2471 gagcgctgcgtgggcgtcacgcggccgctgctccacgccgcgcgggtctcggtcgcccgc 2530
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Qy   2531 gcgcgcctggcgctggccgcggtggccgcggtggccttggccgtggcgctgctgccgctg 2590
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Db    534 GCGCGCCTGGCGCTGGCCGCGGTGGCCGCGGTGGCCTTGGCCGTGGCGCTGCTGCCGCTG 593

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Qy   2831 ggggcgcacggacccccgctcggcctccgcctcgtccgcctcgtccatcgcttcggcctcc 2890
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Db    834 GGGGCGCACGGACCCCGCTCGGCCTCCGCCTCGTCCGCCTCGTCCATCGCTTCGGCCTCC 893

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Qy   2951 gagatggtgggccagcttgtcggtatcatggtggtgtcgtgcatctgctggagcccaatg 3010
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Db    954 GAGATGGTGGGCCAGCTTGTCGGTATCATGGTGGTGTCGTGCATCTGCTGGAGCCCAATG 1013

Qy   3011 ctggtgaggggcgcaccggcccctcgagccacgctccttcccgctccctctcggc 3065
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Db   1014 CTGGTGTTGGTGGCGCTGGCCGTCGGCGGCTGGAGCTCTACCTCCCTGCAGCGGC 1068


RESULT   5
AR086516
LOCUS       AR086516               1394 bp    DNA     linear   PAT 07-SEP-2000
DEFINITION  Sequence 3 from patent US 5985597.
ACCESSION   AR086516
VERSION     AR086516.1  GI:10013282
KEYWORDS    .
SOURCE      Unknown.
  ORGANISM  Unknown.
            Unclassified.
REFERENCE   1  (bases 1 to 1394)
  AUTHORS   Ford-Hutchinson,A., Funk,C., Grygorczyk,R. and Metters,K.
  TITLE     DNA encoding prostaglandin receptor EP1
  JOURNAL   Patent: US 5985597-A 3 16-NOV-1999;
FEATURES             Location/Qualifiers
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BASE COUNT      157 a    525 c    484 g    228 t
ORIGIN


  Query Match             24.7%;  Score 967;  DB 6;  Length 1394;
  Best Local Similarity   97.0%;  Pred. No. 9.7e-101;
  Matches  985;  Conservative    0;  Mismatches   30;  Indels    0;  Gaps    0;

Qy   2051 ccagcacccctggcgcctgacatgagcccttgcgggcccctcaacctgagcctggcgggc 2110
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Qy   2111 gaggcgaccacatgcgcggcgccctgggtccccaacacgtcggccgtgccgccgtcgggc 2170
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RESULT 6
AX280933
LOCUS AX280933 1209 bp DNA linear PAT 02-NOV-2001
DEFINITION Sequence 556 from Patent WO0177172.
ACCESSION AX280933
VERSION AX280933.1 GI:16608222
KEYWORDS .
SOURCE human.
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (sites)
AUTHORS Lehmann-Bruinsma,K., Liaw,C.W. and Lin,I.L.
TITLE Non-endogenous, consstitutively activated known g protein-coupled
receptors
JOURNAL Patent: WO 0177172-A 556 18-OCT-2001;
Arena Pharmaceuticals, Inc. (US)
FEATURES Location/Qualifiers
source 1. .1209
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BASE COUNT 107 a 469 c 424 g 209 t
ORIGIN

Query Match 24.1%; Score 944.4; DB 6; Length 1209;
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Matches 963; Conservative 0; Mismatches 31; Indels 0; Gaps 0;

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Qy   2672 gcactgcttgctggcctcttcgccagcctcggcctggtcgcgctcctcgccgcgctggtg 2731
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          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    781 GCCTCCGCCTCGTCCGCCTCGTCCATCGCTTCGGCCTCCACCTTCTTTGGCGGCTCTCGG 840

Qy   2912 agcagcggctcggcacgcagagctcgcgcccacgacgtggagatggtgggccagcttgtc 2971
          ||||||||||||||||||||||||||||||||||||||||||  ||||||||||||||
Db    841 AGCAGCGGCTCGGCACGCAGAGCTCGCGCCCACGACGTGGAGATGAAGGGCCAGCTTGTC 900

Qy   2972 ggtatcatggtggtgtcgtgcatctgctggagcccaatgctggtgaggggcgcaccggcc 3031
          ||||||||||||||||||||||||||||||||||||||||||  ||  || | ||||
Db    901 GGTATCATGGTGGTGTCGTGCATCTGCTGGAGCCCAATGCTGGTGTTGGTGGCGCTGGCC 960

Qy   3032 cctcgagccacgctccttcccgctccctctcggc 3065
              | | |  |  |  | || | |     ||||
Db    961 GTCGGCGGCTGGAGCTCTACCTCCCTGCAGCGGC 994
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